Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/594,595	**Applicant(s)** KATO ET AL.	
	Examiner Shin-Lin Chen	**Art Unit** 1632	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 09 July 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *None*.
   Claim(s) objected to: *None*.
   Claim(s) rejected: *8,9,11,13-15,17 and 18*.
   Claim(s) withdrawn from consideration: *1-7*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Shin-Lin Chen/
Primary Examiner, Art Unit 1632

Continuation of 11. does NOT place the application in condition for allowance because: Applicant argues that the recited growth factors show efficiency in inducing mesenchymal stem cell migration, Example 4 is commesurate with at least claims 13 and 15 that the stem cell factor is administered to the site where accumulation of the mesenchymal stem cells is desired. The newly added claim 19 recites administering the growth factor with atelocollagen into the injured tissue. Applicant further argues that the administration of the stem cells into the tail vein in an animal model represents the most dispersive mode of administration and the injected stem cells are localized to the injection site of the growth factors, which demonstrates that the claimed invention is enabled and no undue experimentation is required (amendment, p. 5-7). This is not found persuasive because of the reasons of record. The term "topically" (claims 13 and 15) means applying themedicine to body surfaces. It is unclear how to apply the migration-enhancing factor topically to the injured tissue when the injured tissue is deep inside the body. The claims (except new claim 19) read on administering the mesenchymal stem cell-enhancing factor via various administration routes. The art of delivering a protein complex to various target sites in vivo was unpredictable at the time of the invention. There are various barriers before a protein can reach its target cells, for example, layers of dermal cells, blood vessel wall cell membranes, proteases and lysosomal degradation within cells, extracellular matrix between cells, gastrointestinal digestive acids, and blood-brain barrier for reaching cells in the brain. Whether the protein can reach target cells in vivo or not depends on the administration route of said protein. The claimed invention is "a method of regeneration therapy for injured tissue", which requires regeneration of the injured tissue. Although mesenchymal stem cells administered via tail vein can be localized to the injection site of growth factors, it is unclear whether sufficient MSCs can be obtained at the target injured tissue so as to provide regeneration therapy for injured tissue in vivo. The specification fails to provide adequate guidance and evidence for whether administration of the claimed factor via various administration routes would be able to reach the target site or injured tissue in a subject and whether sufficient MSCs and the claimed factor can be obtained at the target site or injured tissue so as to enhance regeneration of the injured tissue in vivo. Whether the administered MSCs and claimed factor via various administration routes would be able to enhance regeneration of the injured tissue in vivo was unpredictable at the time of the invention. Absent specification guidance, one skilled in the art at the time of the invention would require undue experimentation to practice over the full scope of the invention claimed. .